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AUTONOMIC NERVOUS FUNCTION OF HAND-ARM VIBRATION SYNDROME PATIENTS

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ABSTRACT

We have investigated the autonomic nervous function of hand-arm vibration syndrome patients using blood chemical analyses and electrophysiological methods. When exposed to whole body cooling, hand-arm vibration syndrome patients showed a significantly greater increase of plasma norepinephrine than the age-matched healthy controls. The patients also exhibited reduced variation of R-R intervals in electrocardiogram during deep breathing. When classifying the subjects according to the Stockholm Workshop scale of VWF, the subjects of stage 3 showed the most remarkable findings followed by the subjects of stage 2. The findings of the stage 3 subjects were also greater than those of diabetes patients. The excess secretion of norepinephrine in blood reveals that the responsiveness of the sympathetic nervous system to cold exposure is enhanced in hand-arm vibration syndrome patients. The R-R interval variation suggests that the basal activity of the parasympathetic nervous system is reduced. We observed that plasma norepinephrine also increased during short-term exposure of hand-arm to vibration and noise exposure potentiated the effect. It seems likely that repeated vibration exposures of the hand-arm system develop the hyperactivity of the sympathetic nervous system.

Key Words: Hand-arm vibration, Autonomic nervous function, Cold exposure, Plasma norepinephrine, Heart rate variation

INTRODUCTION

Vibration induced-white finger (VWF) is the most characteristic symptom in the hand-arm vibration syndrome. In regard to the pathogenesis of vibration-induced white finger, a local mechanism is proposed. Since VWF mainly appears on the skin of the fingers and hands directly exposed to vibration, and only rarely reaches the lower arms exposed to transmitted vibration in a severe case, the role of the local mechanism is assumed to be large.

On the other hand, VWF is usually provoked by a cold sensation when the whole body is exposed to cold. Occasionally, emotional stress and rapid change of atmospheric temperature provoke the appearance of VWF. These facts indicate that the sympathetic nervous system has a role in evoking VWF. Using analysis of heart rate variation and responses of plasma cyclic nucleotides to whole body cooling, we observed the differences in the autonomic function between hand-arm vibration subjects and the healthy controls.[1,2] It has been also pointed out that hand-arm vibration syndrome patients have higher complaint rates of subjective symptoms not localized in the upper limbs.[3]

For investigating the autonomic nervous function and the central nervous function of hand-arm vibration syndrome patients in more detail, we performed a large scale experimental study from November 1987 to March 1988, and reported the results at the Kurume University Symposium on Vibration Stress and the Autonomic Nervous System as well as at the 5th Interna-

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tional Conference on Hand-Arm Vibration.[4,5] In this paper, details of the study methods, the findings of the subjects limited to the current workers without medical treatment and some issues related to the significance of the findings have been discussed.

METHODS AND SUBJECTS

Table 1 shows the criteria for selecting subjects. For the VWF(+) group, subjects, experiencing typical white finger attacks, a few times per week during the previous winter, were chosen. For the VWF(−) group, subjects, who had never had a history of white finger but had other hand-arm symptoms, such as numbness or pain, were chosen. For the VWF(+) group, the VWF(−) group and the control group, subjects being given drug therapy except for hand-arm vibration syndrome were excluded. Subjects with complicated diseases such as pneumoconiosis, diabetes mellitus, hypertension, heart disease, liver disease or a history of cerebrovascular disease were also excluded. Furthermore, the subjects were individually matched according to age within 5 years among the three groups. The subjects ceasing the operation of vibratory tools were also individually matched according to the years of cessation.

Before selecting subjects, more than 1000 male candidates including healthy controls were listed. We checked these lists and chose about 500 candidates. Using telephone, we interviewed them about their symptoms and medical history. As a result, approximately 300 subjects were selected and examined. Then, 70 matched sets were obtained after individual matching. Among them, 36 sets were constituted by current workers without medical treatment. In this paper, the results of these 36 matched sets are reported, because they had not the effects of period after ceasing the operation of vibratory tools as well as medical therapy for a long time.

On the other side, 23 diabetes patients were also examined. Diabetes patients occasionally have autonomic nervous findings, therefore the findings of the diabetes group were compared with those of the hand-arm vibration syndrome group. About half of the diabetes patients were on drug therapy while the others underwent a dietetic treatment.

Mean age, body height and body weight were not significantly different among the groups except for body weight in VWF(+) group, as shown in Table 2. Although the years of exposure to vibration were no different between the VWF(+) and the VWF(−) groups, accumulated hours

Table 1. Criteria for selecting subjects

VWF(+) group
1. typical VWF attacks with frequency of two or more times per week in winter
2. 4000 hours or more of accumulated hours of vibration exposure
VWF(−) group
1. hand-arm symptoms induced by vibration exposure but no history of white finger
2. 4000 hours or more of accumulated hours of vibration exposure
VWF(+), VWF(−) and control groups
1. no drug therapy
2. no complicated diseases
individual matching
1. age matching for VWF(+), VWF(−) and control
2. matching of years after ceasing vibratory tool operation for VWF(+) and VWF(−)

of exposure in the VWF(+) group were larger than those in the VWF(−) group. Most of the subjects exposed to vibration in the VWF(+) and VWF(−) groups were working in forestry (40.3%) and construction industries (34.7%). The most common tools operated were chain-saws (41.7%) followed by pneumatic hammers and drills (26.4%).

Table 3 shows smoking habits and alcohol consumption. History of cigarette smoking tended to be longer in the VWF(+) group and the VWF(−) group than those in the control group. However, Brinkmann indices did not show significant differences between the VWF(+) group, the VWF(−) group and the control group. Estimated alcohol consumption was also no different among the VWF(+) group, the VWF(−) group and the control group.

Table 4 shows the examination program. Medical history and subjective symptoms were interviewed by medical doctors. Subjects with abnormal findings on clinical examination were excluded from analysis. For investigating autonomic nervous functions, cold exposure test of the whole body and electrophysiological tests referred to Ewing's methods, were performed.[6] Except for occupational history, all examinations were done under blind condition. Seven days before the tests, all drug treatments were terminated to eliminate any effects of drugs on the examination.

Table 2. Number of subjects, their age, body dimensions, years of exposure to vibration and accumulated hours of exposure

group	n	age (yr)	height (cm)	weight (kg)	years of exposure	hours of exposure (100h)
VWF(+)	36	54.3±5.3	162.2±5.7	57.8±6.6*	22.3±7.6	187±114#
VWF(−)	36	53.7±5.0	160.4±7.6	59.5±8.9	21.3±7.7	117± 86
control	36	54.1±5.6	161.3±5.8	61.4±7.6		
diabetes	23	56.7±5.6	163.3±5.3	62.3±8.0		

Mean±SD;

* $p<0.05$ compared with control group, # $p<0.05$ compared with VWF(−) group.

Table 3. Smoking habit and alcohol consumption

	n	smoking history		alcohol consumption	
		years	BI#	years	amount##
VWF(+) group	36	29.6±13.1	604±510	21.4±14.0	348±290
VWF(−) group	36	28.3±14.2	593±475	19.0±14.4	364±391
control group	36	24.4±15.4	561±431	20.2±15.3	392±655
diabetes group	23	23.4±15.0	677±503	21.8±13.8	422±364

Mean±SD

BI: Brinkmann index (number of cigarettes per day multiplied by years).

amount: accumulated consumption (liter).

Table 4. Examination program

1. occupational and medical history
2. subjective symptoms
3. physical examination
4. clinical examination
   analyses of blood and urine, chest XP, ECG, funduscopy, etc.
5. cold exposure test
   plasma catecholamines, cyclic nucleotides, other hormones, etc.
6. electrophysiological tests
   Valsalva test, ECG R-R variance, hand-grip test, etc.
7. other
   EEG, sleep EEG, ABR, etc.

RESULTS

Subjective symptoms

Among the 36 subjects in the VWF(+) group, 22 subjects had a history of 8 white fingers or more. Four subjects had experienced white attack up to hands. According to the Stockholm Workshop scale of VWF,[7] 11 subjects were classified as stage 3 (SW-3) and 25 subjects as stage 2 (SW-2). More than half of the subjects in the VWF(+) group and in the VWF(−) group had moderate or severe numbness.

Table 5 shows the subjective symptoms not localized in the upper limbs. The VWF(+) group and the VWF(−) group had higher prevalence rates of most symptoms than the control group. The diabetes group had higher prevalence rates of sexual disinclination and forgetfulness.

Table 5. Subjective symptoms not localized to the limbs (%)

group n	VWF(+) 36	VWF(−) 36	control 36	diabetes 23
headache	4(11)	12(33)*	4(11)	1(4)
head-heaviness	6(17)	13(36)*	4(11)	4(17)
insomnia	14(39)*	16(44)**	5(14)	6(26)
cold-feeling	23(64)**	18(50)*	8(22)	5(22)
sexual disinclination	8(22)	8(22)	3(8)	11(48)**
forgetfulness	17(47)**	16(44)**	5(14)	9(39)*
irritability	7(19)	12(33)	8(22)	5(22)

Mean ± SD; * $p < 0.05$, ** $p < 0.01$ compared with control group.

Cold exposure test

During the cold exposure test, blood samples were taken under two conditions. First, the subject was required to sit in a room at a temperature of 25 ± 1°C and blood was drawn after 25 minutes. Then the subject moved and sat in a cold room in which the temperature was controlled at 7 ± 1.5°C and blood was drawn after 25 minutes. For this test, the subjects wore two pieces of clothing on the upper and lower half of the body. Under the atmospheric temperature of 25°C, blood pressure and finger skin temperature were not significantly different. The decrease of skin temperature during the cold exposure test was largest in the VWF(+) group, especially in the stage 3 subgroup of Stockholm Workshop scale. The increase of diastolic blood pressure in the VWF(+) group and the VWF(−) group tended to be larger than that in the control group.

Table 6 shows the changes of plasma norepinephrine levels during the cold exposure test. Plasma norepinephrine is maintained by release from the sympathetic nerve endings and is a sensitive indicator of sympathetic nervous function. The level of plasma norepinephrine increased during exposure to cold in all groups. The percentage of increase was largest in the VWF(+) group followed by the VWF(−) group. In the VWF(+) group, the increase in the stage 3 subgroup of Stockholm Workshop scale was larger than that in the stage 2 subgroup.

Cyclic GMP are second messengers in cells, and responses of the plasma level to physiological stress are pointed out to reflect the autonomic nervous function. When exposed to cold, significant increase of plasma cyclic GMP level was observed in the hand-arm vibration syndrome patients.[2,8] As shown in Table 7, the level of plasma cyclic GMP increased during exposure to

Table 6. Responses of plasma norepinephrine levels (pg/mℓ) during cold exposure test of the whole body at 7°C

	n	rest	exposure	% increase
VWF(+) group	36	319 ± 124	1039 ± 401	244 ± 123**
SWs stage-3	11	297 ± 67	1049 ± 299	255 ± 69**
SWs stage-2	25	329 ± 143	1035 ± 444	239 ± 142*
VWF(−) group	36	318 ± 120	927 ± 378	201 ± 93
control group	36	350 ± 117	913 ± 319	167 ± 73
diabetes group	23	272 ± 117*	848 ± 355	229 ± 117*

Mean ± SD; * $p < 0.05$, ** $p < 0.01$ compared with control group.

Table 7. Responses of plasma cyclic GMP levels(pmol/mℓ) during cold exposure test of the whole body at 7°C

	n	rest	exposure	% increase
VWF(+) group	36	3.0 ± 1.1	3.9 ± 1.9*	37 ± 75
SWs stage-3	11	2.8 ± 0.8	4.1 ± 2.5	51 ± 98
SWs stage-2	25	3.1 ± 1.2	3.8 ± 1.6	32 ± 64
VWF(−) group	36	2.8 ± 1.6	3.4 ± 2.4	35 ± 108
control group	36	2.7 ± 1.6	3.0 ± 1.6	22 ± 47
diabetes group	23	2.9 ± 1.5	3.3 ± 1.9	20 ± 52

Mean ± SD; * $p < 0.05$ compared with control group.

cold in all groups. The percentage of increase tended to be larger in the VWF(+) group and the VWF(−) group than in the control group. However, the differences were not statistically significant.

Heart rate tests

Table 8 shows the results of heart rate tests to Valsalva manoeuvre, deep breathing and standing. The figures indicate the number of subjects with reduced response. Valsalva test was performed by asking the subjects to blow into a mouthpiece attached to an aneroid pressure gauge at a pressure of 40 mmHg for 15 seconds. The ratio of the longest R-R interval shortly after the manoeuvre to the shortest R-R interval during the manoeuvre was evaluated. The diabetes group tended to have a lower Valsalva ratio, but no other differences were observed. For R-R interval variation tests, serial 100 beats at deep breathing and standing were calculated. Deep breathing consisted of 5 seconds of inspiration followed by 5 seconds of expiration. The VWF(+) group and the diabetes group had a larger percentage of subjects with reduced coefficient of variation at deep breathing.

Table 8. Number of subjects with reduced heart rate responses to Valsalva manoeuvre, deep breathing and standing(%)

group		VWF(+)			VWF(−)	control	diabetes
			SWs-3	SWs-2			
n		35	10	25	36	36	23
Valsalva ratio	< 1.21	5(14)	2(20)	3(12)	3(8)	5(14)	8(35)
CV at deep-breathing	< 3.5%	12(34)*	5(50)*	7(28)	9(25)	4(11)	8(37)*
CV at standing	< 3.5%	12(34)	4(40)	8(32)	12(33)	7(19)	11(48)*

* $p < 0.05$ compared with control group.

DISCUSSION

In regard to the greater prevalence of subjective symptoms not localized in the upper limbs, psychosomatic effects resulting from long term medical therapy might be considered. We observed that the hand-arm vibration syndrome patients under medical treatment tended to have a larger prevalence rate of subjective symptoms than the current workers exposed to vibration. However, we also confirmed that the current workers exposed to vibration not under medical treatment had higher prevalence rates of subjective symptoms, such as head-heaviness, insomnia, forgetfulness and so on than the control workers.

The summary of representative findings in this study is shown in Fig. 1. Hand-arm vibration syndrome subjects had larger prevalence rates of subjective symptoms not localized in the upper limbs than the healthy controls. They also showed greater responses to whole body cooling and reduced responses of heart rate variation tests. The former findings suggest that the responsiveness of the sympathetic nervous system to cold exposure is enhanced in hand-arm vibration syndrome patients; the latter findings suggest that the basal activity of the parasympathetic nervous system is reduced.

These findings tended to correlate with the severity of vascular symptoms evaluated with the

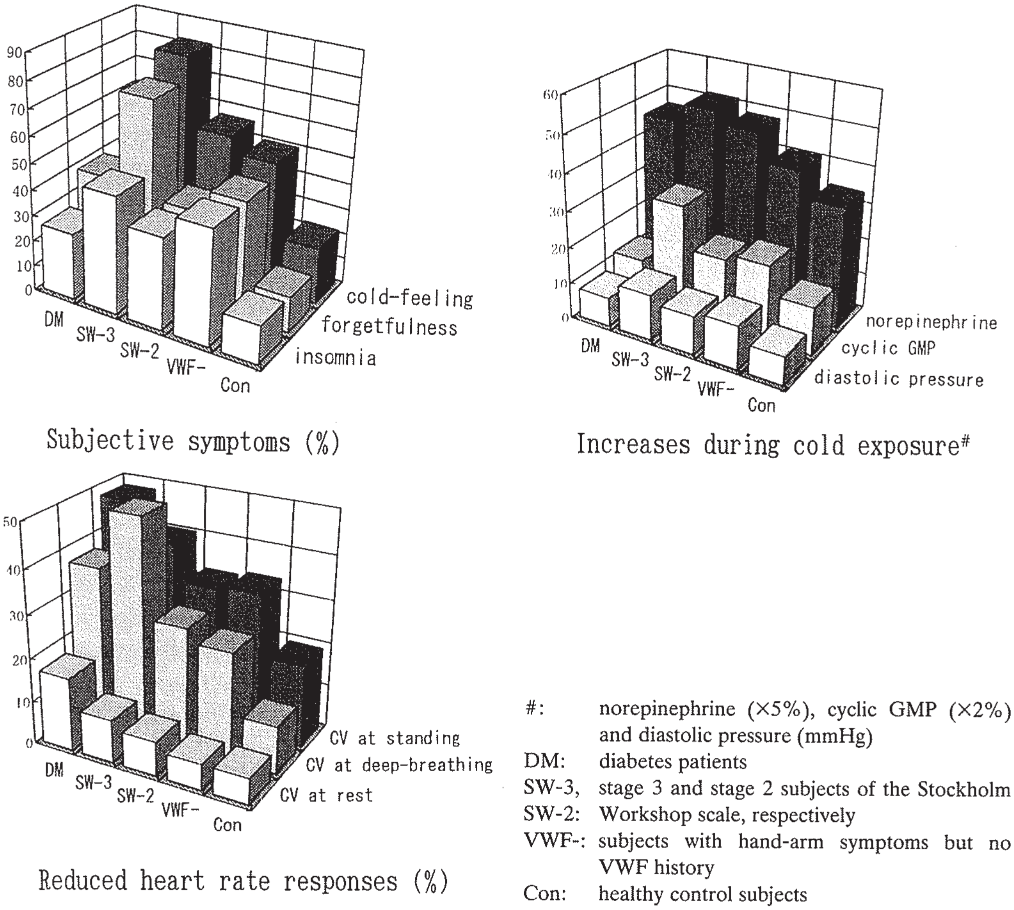

Fig. 1. Summary of representative results

Stockholm Workshop scale. We tried the same analysis using the sensorineural stage of the hand-arm vibration syndrome proposed by Brammer et al.,[9] however, significant correlations between the autonomic findings and the severity of sensorineural symptoms was not observed. As our data was not enough to classify the subjects according to the sensorineural scale, it is not yet concluded whether the autonomic findings are related to vascular symptoms rather than sensorineural symptoms.

Autonomic neuropathy is established as a common complication of diabetes mellitus. Mean value of HBA_1 in the diabetes patients investigated in our study was 8.9% (min 6.0, max 12.1). Although the diabetes group did not include very severe cases, medical controls of diabetes were fair or poor in half of patients. They showed similar autonomic findings to the hand-arm vibration syndrome subjects, however the severity was smaller than the stage 3 subjects of the Stockholm Workshop scale. This fact suggests that autonomic finding in severe cases of the hand-arm vibration syndrome is greater than that of the diabetes patients in ordinary stage.

At the 6th International Conference of Hand-Arm Vibration, we reported the effects of acute exposure of hand-arm vibration on the sympathetic nervous system.[10] Four healthy subjects were exposed to vibration and/or noise for ten minutes under different atmospheric temperatures at 25°C and 13°C. Blood samples via a catheterized forearm vein were taken and plasma catecholamines were analyzed. Exposure to noise alone did not induce a significant increase of the plasma norepinephrine level. During vibration exposure, the plasma norepinephrine level gradually increased, and noise exposure potentiated the effect, which implies a synergistic effect.

It was also reported that skin sympathetic activity in the lower extremities increased when a hand was exposed to vibration for a short term.[11] It seems likely that repeated vibration exposures of the hand-arm system develop the hyperreactivity of the sympathetic nervous system. It is pointed out that the direct effect of short-term vibration exposure on isolated vascular smooth muscle is inhibition of the contraction. If this is true, the effect may exaggerate the hyperresponse of the sympathetic nervous system. Noise and cold exposure during vibratory tool operation also can potentiate development of the hyperreactivity.

Several problems are yet to be solved. It is pointed out that the subjects with autonomic findings might have a constitutional disposition. Our investigation method is a cross-sectional study as well as most other investigations concerning the pathogenesis of hand-arm vibration syndrome. For answering this kind of question, longitudinal epidemiological studies are needed in future.

Whether the autonomic nervous findings have clinical significance or not, is another problem. The stage 3 subjects of the Stockholm Workshop scale showed greater findings of the autonomic nervous tests than the diabetes patients. Although we cannot provide an conclusive answer at present, we suspect a relation between the higher prevalence rates of subjective symptoms not localized in the limbs and the autonomic nervous findings observed in our study. We suppose that excess prevalence rates of the subjective symptoms are possibly induced by the hyperresponsiveness of the autonomic nervous system to various stresses in daily life.

When exposed to whole body cooling, hand-arm vibration syndrome patients showed a significantly greater increase of plasma norepinephrine than the age-matched healthy controls. The excess secretion of norepinephrine in blood reveals that the responsiveness of the sympathetic nervous system to cold exposure is enhanced in hand-arm vibration syndrome patients. The patients also exhibited reduced variation of R-R intervals in electrocardiogram during deep breathing. The R-R interval variation suggests that the basal activity of the parasympathetic nervous system is reduced. These findings tended to correlate with the severity of vascular symptoms evaluated with the Stockholm Workshop scale. Furthermore, the stage 3 subjects showed severer findings than the diabetes patients. The significance of these findings in the pathophysiology of the hand-arm vibration syndrome must be investigated in future.

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